REMARKS

Claims 1-20 are pending in this application. Claims 1-16 have been rejected. Claims 17-20 have been withdrawn from consideration. Claim 7 has been amended. Claims 6 and 17-20 have been canceled. No new matter has been added. Applicants are respectfully requesting reconsideration in view of the following remarks.

I. Information Disclosure Statement

Applicants acknowledge the Examiner's consideration of the Information Disclosure Statements filed December 8, 2006 and July 12, 2006.

II. Election/Restriction Requirement

The restriction requirement placing the claims into Groups I-III has been deemed proper and made final. Claims 17-20 have been withdrawn from consideration. Accordingly, Applicants have canceled claims 17-20 without prejudice reserving the right to file continuing applications for the canceled subject matter.

III. Claim Objections

Claim 7 has been objected to because steps f) and g) relate to the amount of "reporter;" however, it is suggested that it is the amount of reporter protein that would be detected in step f) and used to sort with step g). In an earnest effort to facilitate the prosecution of this application, Applicants have made the appropriate amendment to claim 7. It is therefore respectfully requested that this objection to the claims be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. §102

Claims 1-5 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,665,577 to Sodroski et al. (filed November 1994; issued September 9, 1997). It is suggested that the '577 patent teaches methods of obtaining an enriched population of human hematopoietic cells, separation of hematopoietic cells from a source, separating a subpopulation of cells utilizing a CDw109 antibody (claim 1) and then an additional marker to separate the cells, such as CD34, Thy-1 and rho (claims 2-3). Limitations recited in instant claims 2-5 are suggested to be inherent in the cells of the '577 patent.

Applicants respectfully traverse this rejection. At the outset, Applicants respectfully submit that claim 1 of the '577 patent to Sodroski, et al. is drawn to:

> "1. An HIV vector comprising: (a) a DNA segment from an HIV genome, wherein the DNA segment comprises the HIV gag, pol and env genes; wherein said HIV vector lacks the HIV packaging sequence necessary to package HIV RNA into virions; wherein said HIV packaging sequence is the nucleotide sequence located between the 5' major splice donor site and the initiation codon of the gag gene on the HIV genome; and (b) a promoter operably linked to the DNA segment from an HIV genome of (a); wherein the HIV vector, when introduced into a eukaryotic host cell, express HIV gag, pol and env proteins to form HIV virions that do not contain sufficient HIV RNA to result in a replication competent HIV virion."

Claims 2 and 3 further read:

> "2. The HIV vector claim 1, wherein the promoter is an HIV LTR.
>
> 3. The HIV vector of claim 1, wherein the promoter functions to express genes preferentially in specific cell types."

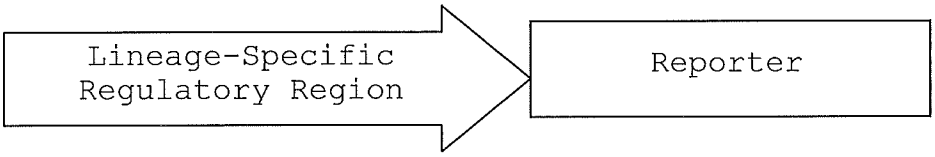
However, nowhere do Applicants find any reference in the cited passages of isolating a self-renewing, multipotent, slow-cycling cell by obtaining a population of cells from a sample and sorting the population of cells based on the presence of CD34 and the amount of a selected slow-cycling cell marker expressed by each cell. Indeed, a cursory word search of the entire '577 patent did not identify a single passage referring to CD34 or a selected slow-cycling cell marker, or use thereof for isolating any cells.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In so far as the '577 patent fails to teach or suggest the method and cells as presently claimed, it is respectfully requested that this rejection be withdrawn.

Claims 9 and 13 have been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,639,618 to Gay. It is suggested that the '618 patent teaches transfection of a pluripotent ES cell with a construct comprising a regulatory region of a lineage specific gene operably linked to DNA encoding a reporter protein and separation of the differentiated lineage-specific stem cell. It is alleged therefore that the cells of the invention are anticipated by the '618 patent.

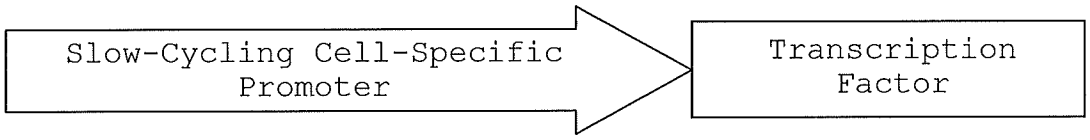
Applicants respectfully traverse this rejection. The '618 patent teaches a cell harboring a construct comprising a regulatory region of a lineage-specific gene operably linked to a DNA encoding a reporter protein. See col. 3, lines 15-20.



Construct of the '618 Patent

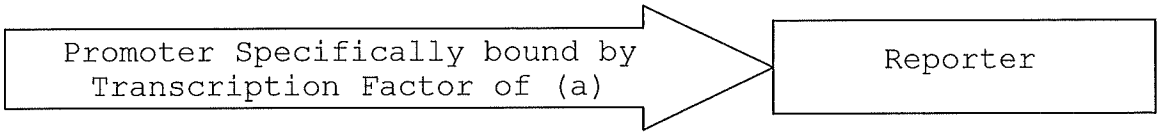
In contrast, the isolated cells of claims 9 and 13 harbor additional nucleic acids not present in the cells of the '618 patent. Moreover, the nucleic acids introduced into the cells of claims 9 and 13 are combined in a manner neither taught nor suggested by the '618 patent. Specifically, as set forth in claim 7, from which claims 9 and 13 depend, the cells of the invention harbor:

(a) a nucleic acid encoding a regulatable transcription factor operably linked to a promoter which is active in a slow-cycling cell; and



Construct (a)

(b) a nucleic acid encoding a reporter protein operably linked to a regulated promoter to which the regulatable transcription factor binds.



Construct (b)

To anticipate a claim, "[t]he identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim, but this is not an *ipsissimis verbis* test,

i.e., identity of terminology is not required. *In re Bond*, 910 F.2d 831, 15 USPQ2d 1566 (Fed. Cir. 1990). In this respect, the cells of the '618 patent fail to contain all of the nucleic acids of the instant cells in the arrangement presently claimed. Therefore, the cells of the '618 patent cannot be held to anticipate the cells of claims 9 and 13. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

Claim 6 has been rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,861,315. It is suggested that the '315 patent teaches a clonal culture of CD34+ hematopoietic stem cells thereby anticipating the present invention.

Applicants respectfully disagree with this rejection. However, in the interest of facilitating the prosecution of this application, Applicants have canceled claim 6. It is therefore respectfully requested that this rejection be reconsidered and withdrawn.

V. Rejection of Claims Under 35 U.S.C. §103

Claims 7 and 9 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,639,618 when taken with Strathdee et al. ((1999) *Gene* 229:21-29), Bohl et al. ((1997) *Nat. Med.* 3:229-305) when taken with Mahmud ((2001) *Blood* 97:3061-3068) and U.S. Patent 6,485,971. It is suggested that the '618 patent provides guidance for using a promoter that is active in stem cells and using known cell sorting techniques (page 7, ¶1 of the Office Action). It is acknowledged that the '618 patent does not however teach steps (a) and (b) of claim 7 (page 7, ¶2 of the Office Action). In this respect, the Examiner asserts that

Strathdee teaches using the tetracycline-responsive system to provide efficient, tightly regulated, inducible gene expression, wherein gene expression can be efficiently switched on and off using doxycyline (page 7, ¶2 of the Office Action). The Examiner further asserts that Bohl teaches using tetracycline regulation of gene expression for muscle-specific expression of mouse erythropoietin cDNA using a two vector system, wherein control of rtTA expression from a skeletal muscle-specific promoter prevents the accumulation of the potentially toxic protein in vector-producing cells and that the resultant cells stably expressed the vector over time (page 7, ¶2 of the Office Action). The Examiner acknowledges that neither the '618 patent, Strathdee nor Bohl specifically teach steps (d)-(g) of instant claim 7 (page 8, ¶2 of the Office Action). It is asserted however that Mahmud et al. provide specific guidance to show that multipotent stem cells are considered slow cycling cells and the concept of separating rapidly dividing cells from slow cycling cells is known in the art as evidenced by the '971 patent (page 8, ¶2 of the Office Action). The Examiner concludes that the '618 patent provides guidance with regard to isolation of lineage-specific cells, and both Strathdee and Bohl teach methods of inducible gene expression that can efficiently be switched on and off, and avoid the art-recognized problem of toxicity (page 8, ¶3 of the Office Action). It is further concluded that Strathdee provides motivation for utilizing this type of system in specific cell types and Bohl provides guidance to show that, using a cell-specific promoter, one can efficiently express a gene of interest in a cell type of interest, wherein Mahmud and the '971 patent provide sufficient guidance to show that one of skill in the art

would be readily apprised that stem cells are considered slow-cycling, and the '971 patent provides sufficient guidance to separate cells based on the amount of reporter gene expression (page 8, ¶3 of the Office Action). The Examiner contends that one of skill would have been motivated to, in view of the teachings of Mahmud and the '971 patent, to inactivate the regulatable transcription factor and select for slow-cycling stem cells by allowing the cells to divide, and selecting cells that contain a higher level of reporter protein expression.

Applicants respectfully traverse this rejection. In *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the Court reasoned that the analysis under 35 U.S.C. § 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418; *see also id.* at 421 ("A person of ordinary skill is ... a person of ordinary creativity, not an automaton."). While it emphasized a flexible approach, the Court nonetheless reaffirmed that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id.* at 418.

Rather, as the Court stated:

> [I]t can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements *in the way the claimed new invention does* ... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Id. at 418-419 (emphasis added); *see also id.* at 418 (requiring a determination of "whether there was an apparent reason to combine the known elements *in the fashion claimed* by the patent at issue") (emphasis added).

Accordingly, the courts have held, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

In the present case, the Examiner has relied upon Mahmud and the '971 patent to teach the features set forth in steps (d)-(g) of instant claim 7. However, Applicants respectfully submit that there is simply no teaching or suggestion in any of the cited references of the combination of elements set forth in steps (d)-(g) of instant claim 7. While Mahmud et al. appear to teach the incorporation of BrdU into pluripotent hematopoietic stem cells to analyze the replicative history of the same (abstract), and the '971 patent appears to teach separation of cells based upon the level of transferrin receptor, epidermal growth factor receptor, insulin growth factor receptor and keratinocyte growth factor receptor expressed by a cell (claim 1), this does not constitute sufficient guidance for the steps of (d) inactivating the regulatable transcription factor so that expression of the reporter protein is decreased; (e) incubating the cell for a sufficient amount of time so that the cell goes through one or more cell cycles to generate a population of cells; (f) detecting the amount of reporter protein in the population of cells; and (g) sorting the population of cells by the amount of reporter protein present in each cell, as required by instant claim 7.

In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art. *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992).

A mere conclusory statement that it would have been obvious to inactivate the regulatable transcription factor and select for slow-cycling stem cells by allowing the cells to divide, and selecting cells that contain a higher level of reporter protein expression is not sufficient to establish a *prima facie* case of obviousness under 35 U.S.C. 103(a). Therefore, the Examiner has not met the initial burden and it is respectfully requested that this rejection be reconsidered and withdrawn.

Claims 8 and 10-14 have been rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,639,618 when taken with Strathdee et al. and Bohl et al. when taken with Mahmud and U.S. Patent 6,485,971 as applied to claims 7 and 9, and further in view of U.S. Patent No. 5,665,577. The Examiner acknowledges that the '618 patent, Strathdee, Bohl, Mahmud and the '971 patent do not teach sorting the population of cells based on the presence of CD34 and the amount of a selected slow-cycling cell marker; however, it is suggested that the '577 patent teachings obtaining an enriched population of hematopoietic stem cells using a CDw109 antibody and an addition marker such as CD34.

Claims 15-16 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Strathdee et al. and Bohl, et al. when taken with Mahmud et al. and U.S. Patent No. 6,485,971 and U.S. Patent No. 5,665,577 as applied to claims 7-14 above, and further in view of U.S. Patent No. 5,861,315. The Examiner acknowledges that the combined teachings of Strathdee, Bohl, Mahmud, the '971

patent and the '577 patent do not specifically teach or suggest a clonal population that comprises the cells of claims 9 or 10. It is suggested, however, that prior to the time of the claimed invention, the '315 patent provided the clonal culture of CD34+ hematopoietic stem cells (col. 6, line 5+).

Applicants respectfully traverse the rejection of claims 8 and 10-16 in view of the cited documents. As indicated above, the teachings of the '618 patent, Strathdee, Bohl, Mahmud and the '971 patent are insufficient to establish a *prima facie* case obviousness as they simply fail to teach or suggest each and every element of base claim 7. In so far as the '577 patent teaches packaging defective and packaging proficient HIV vectors and the '315 patent merely teaches CD34 selection, these references fail to compensate for the deficiencies in the teachings of the primary references. In addition, the '577 patent fails to teach or suggest the subject matter set forth in dependent claims 8 and 10-14. Thus, the combined teachings of the cited references cannot be held to make the subject matter of claims 8 and 10-16 obvious. It is therefore respectfully requested that these rejections under 35 U.S.C. 103(a) be reconsidered and withdrawn.

VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly,

favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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